

**To Cite:**

Novychenko S, Kovalenko S, Lytvyniuk N, Yasynska E, Skrynychuk O, Roborchuk S, Shchudrova T, Unguryan T. Dynamics of respiratory ventilation function indices in patients with chronic obstructive pulmonary disease and bronchial asthma with comorbid irritable bowel syndrome. Medical Science, 2021, 25(115), 2145-2151

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**Peer-Review History**

Received: 03 July 2021

Reviewed & Revised: 06/July/2021 to 16/August/2021

Accepted: 17 August 2021

Published: August 2021

**Peer-review Method**

External peer-review was done through double-blind method.

## Dynamics of respiratory ventilation function indices in patients with chronic obstructive pulmonary disease and bronchial asthma with comorbid irritable bowel syndrome

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**ABSTRACT**

The article presents the study of the respiratory function in patients with chronic obstructive pulmonary disease (COPD) and bronchial asthma (BA) with comorbid irritable bowel syndrome (IBS). We studied the ventilation function of external respiration (FER) and the nature of its changes in response to bronchodilator in COPD and BA with comorbid IBS patients. In patients with COPD, there was a decrease in both FEV1 and FVC. The degree of spirometric disorders correlated with the severity of the disease. The obstructive type of graphic image of the curve "flow-volume", which was characterized by a decrease in the volume velocity of the airflow, was observed in all patients. The ratios of FEV1/FVC % and MEF 25%-75% were reduced in all patients with COPD. The comorbid IBS in patients with moderate BA makes it impossible to achieve complete control over the course of BA due to the persistent spasm of the peripheral bronchi, which requires increased inhalation therapy. Based on the results, in patients with COPD and IBS, the predominance of the peripheral type of persistent generalized bronchial obstruction was revealed. Transient generalized obstruction syndrome prevailed in patients with BA and IBS, completely reversible obstruction – in BA patients without IBS, and maintenance of the peripheral bronchi spasm in BA patients with IBS.

**Keywords:** bronchial asthma, chronic obstructive pulmonary disease, irritable bowel syndrome, respiratory function



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## 1. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) and bronchial asthma (BA) refer to diseases of the bronchial-pulmonary system, which diagnostic criteria are inflammation with formation of bronchial obstruction (Feshchenko, 2018; GINA, 2019; GOLD, 2019; Salama et al. 2020). The main diagnostic method of bronchial obstruction is examination of external respiration function (ERF) – computerized spirometry with the analysis of “flow-volume” curve (Alzahrani & Becker, 2016; Gurung et al., 2011; Habukawa et al., 2013; Kovalenko et al., 2017). Combination of gastroenterological diseases with COPD and BA in recent years has become of an important value. Such kind of combination determine clinical peculiarities of the course of both diseases, which can complicate the situation, provide torpidity to treatment, and deteriorate prognosis (Khristich, 2006; Ojha et al., 2018; Vutcovici et al., 2016).

One of the frequently diagnosed functional gastrointestinal diseases is irritable bowel syndrome (IBS) with high population prevalence (5-24%). IBS considerably affects quality of life and imposes a profound burden on patients and the healthcare system (Defrees & Bailey, 2014; Enck et al., 2016). In our opinion, investigation of interrelations and interdependence of ERF changes in patients suffering from COPD and BA with and without comorbid IBS is rather interesting.

Objective of the study was to investigate respiratory function ventilation and character of its changes in response to a bronchodilator in patients with COPD and BA with comorbid IBS.

## 2. MATERIALS AND METHODS

The study was conducted at the Pulmonology Department of the Chernivtsi Regional Clinical Hospital” (Chernivtsi, Ukraine) in 2019-2020. Fifty patients with COPD, 50 patients with BA, 50 patients with COPD and comorbid IBS, and 50 patients with BA and comorbid IBS during the period of exacerbation of the primary disease were examined. The age of patients was from 24 to 65, including 115 men and 85 women. The diagnosis of the primary and comorbid diseases was made according to the appropriate standards (Dalrymple & Bullock, 2008; GINA, 2019; GOLD, 2019). The patients were examined for the ventilation respiratory function with analysis of the flow-volume curve and on the computerized spirometry. In 64 patients (64%) with COPD post-broncholytic forced expiratory volume in 1<sup>st</sup> second (FEV<sub>1</sub>) was 50-70% from the appropriate one. In 54 patients (36%) post-broncholytic FEV<sub>1</sub> was ≤ 50%. The study did not include patients with FEV<sub>1</sub> less than 30% from the appropriate one, and those with pronounced restrictive disorders – forced vital capacity of the lungs (FVC) less than 65% from the appropriate one. To determine obstruction reversibility the tests with the inhaled bronchodilator salbutamol was used, and its effect on the FEV<sub>1</sub> was assessed. The bronchodilator response (BR) was assessed considering the predicted value for FEV<sub>1</sub>:

$$BR (\%) = \frac{FEV_1 \text{ dil} - FEV_1 \text{ in}}{FEV_1 \text{ pred}},$$

Where FEV<sub>1</sub> in – initial test score before bronchodilation, FEV<sub>1</sub> dil – after bronchodilation, FEV<sub>1</sub> pred – predicted value

## 3. RESULTS

COPD patients presented decrease of both FEV<sub>1</sub> and FVCL. The rate of spirometric disorders correlated with severity of the disease. Post-bronchodilation value of FEV<sub>1</sub><80% from the appropriate one in the combination with FEV<sub>1</sub>/FVCL < 70% (Hensler test) confirmed restriction of the airflow speed available which is not completely reversible. FEV<sub>1</sub>/FVCL ratio is the most susceptible index of airflow rate restriction, and FEV<sub>1</sub>/ FVCL < 70% was considered as an early sign of this disorder in those patients with normal FEV<sub>1</sub> (>80%). Post-broncholytic FEV<sub>1</sub> was measured, which is more reliable prognostic sign than pre-broncholytic FEV<sub>1</sub> (Table 1, 2).

**Table 1** Parameters of the expiratory respiration ventilation function of COPD patients and patients with COPD and IBS

Parameter	COPD (n=100)			COPD with IBS (n=50)		
	predicted value	test score	% of predicted value	predicted value	test score	% of predicted value
TV (tidal volume)	0.65	0.74	113.8±4.3	0.63	0.78	123.8±0.2*
RR (respiratory rate)	20	22.2	111.3±2.6	20	22.53	112.6±2.5
TV/min	13.1	18.2	138.9±3.4	12.67	18.56	146.4±1.6*

IRV (inspiratory reserve volume)	1.25	0.79	63.1±2.5	1.28	0.61	47.6±0.3 *
IVC (inspiratory vital capacity)	4.34	3.95	91.01±1.6	4.4	3.43	77.9±0.4*
IVC (expiratory vital capacity)	4.23	2.47	58.3±1.7	4.33	2.26	52.1±0.3*
VC (vital capacity)	4.56	3.76	82.4±2.4	4.41	3.62	82.0±0.6
FVC (forced vital capacity)	4.56	3.74	82.0±2.1	4.66	3.45	74.0±0.7*
FEV1 (forced expiratory volume in 1 <sup>st</sup> sec)	3.62	2.33	60.0±1.5	3.55	2.10	58.2±0.5
Gensler index	79.3	71.5	78.9±1.9	81.2	72.4	89.1±1.7*
Tiffno index	80.3	57.6	88.1±1.3	76.1	60.8	86.5±1.6
MEF25 (maximal expiratory flow)	4.89	2.83	49.5±2.6	4.92	2.22	45.1±0.4*
MEF50	4.78	2.43	57.8±2.4	4.79	2.23	46.5±0.7*
MEF75	4.23	1.56	36.8±2.4	4.43	1.42	32.0±0.4*
MEF25/75	4.63	2.27	49.02±2.3	4.71	1.95	41.5±0.3*
PEF (peak expiratory flow)	6.67	3.86	57.8±1.7	7.23	3.54	48.9±1.3*
MVV (maximal voluntary ventilation)	114.34	66.21	57.9±2.5	113.1	62.2	54.9±5.2

\* p<0.05 compared with COPD group

All the groups of patients were characterized by an obstructive pattern of “flow-volume” curve with decreased volumetric rate of airflow. FEV<sub>1</sub>/FVC ratio and maximal expiratory flow (MEF<sub>25/75</sub>) were reduced in all COPD patients. Usually FVC was within the normal values or reduced (35%) depending on the effect of pathological process on other lung volumes. In patients with moderate BA in case of moderate obstruction, FVC in the majority of patients (92%) was within the norm, though spirometric data were indicative of obstruction of the respiratory tract (reduced FEV<sub>1</sub>/FVC) in all the patients.

**Table 2** Parameters of the expiratory respiration ventilation function in BA patients and patients with BA and IBS

Parameter	BA (n=100)			BA with IBS (n=50)		
	predicted value	test score	% of predicted value	predicted value	test score	% of predicted value
TV (tidal volume)	0.75	0.72	96.0±2.4	0.73	0.71	97.2±0.4
RR (respiratory rate)	18	20.1	111.6±1.8	18	21.23	117.9±1.7*
TV/min	12.4	15.3	123.3±2.3	12.5	15.43	114.4±1.3 *
IRV (inspiratory reserve volume)	1.44	0.83	57.6±1.6	1.38	0.75	54.3±0.6 *
IVC (inspiratory vital capacity)	4.56	4.21	92.3±1.2	4.53	4.12	90.9±0.5*
IVC (expiratory vital capacity)	4.44	3.51	79.0±1.4	4.42	3.26	73.75±0.4*
VC (vital capacity)	4.67	4.56	97.6±2.1	4.55	4.43	97.36±0.3
FVC (forced vital capacity)	4.78	4.62	96.6±1.5	4.76	3.78	79.41±0.3*
FEV1 (forced expiratory	3.67	2.50	68.3±1.4	3.7	2.46	66.48±0.6

volume in 1 sec)						
Gensler index	76.7	54.1	70.5±1.2	77.7	65.0	83.6±1.6
Tiffno index	78.5	54.8	69.8±1.2	81.3	55.5	68.26±1.4
MEF25 (maximal expiratory flow)	4.66	2.55	54.72±2.7	4.64	2.46	53.01±0.3
MEF50	4.72	2.33	49.36±2.3	4.74	2.26	47.6±0.5
MEF75	4.44	1.56	35.13±1.3	4.41	1.49	33.7±0.3*
MEF25/75	4.60	2.14	46.52±2.4	4.59	2.07	45.0±0.4*
PEF (peak expiratory flow)	6.56	3.55	54.11±1.3	6.48	3.32	49.8 ±1.2*
MVV (maximal voluntary ventilation)	112.41	69.57	61.8±1.43	112.2	65.4	58.2±4.3*

\* p<0.05 compared with BA group

According to the determined disorders in the ventilation function of the external respiration the patients were divided into the following groups:

1<sup>st</sup> group – patients with isolated obstruction syndrome of the minor bronchi.

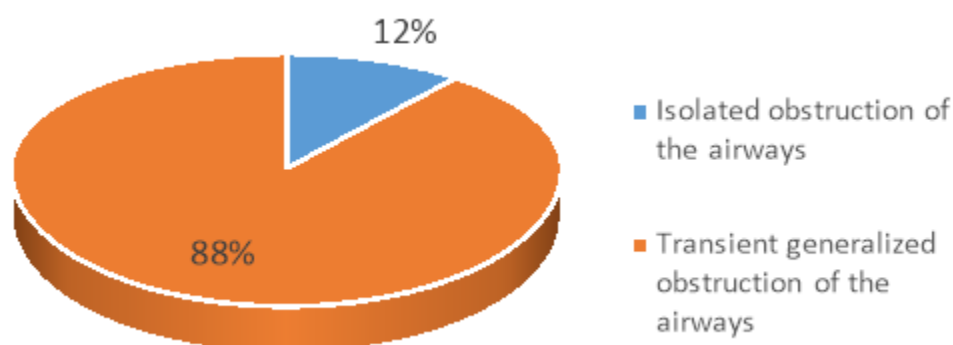
2<sup>nd</sup> group – patients with transient generalized obstruction syndrome.

3<sup>rd</sup> group – patients with stable generalized obstruction syndrome:

a) emphysematous type

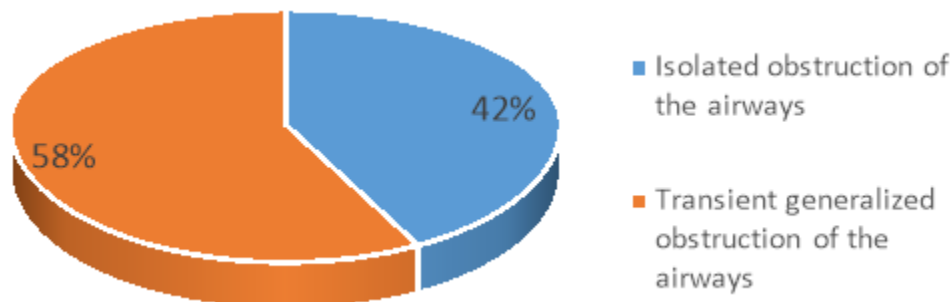
b) bronchial type

The first group of patients with isolated obstruction syndrome of the minor bronchi included 12 (12%) individuals with mild BA without IBS and 42 (42%) individuals with BA and IBS. The course of the underlying disease of these patients was mild. Examination of external respiration function (ERF) during the period of BA remission diagnosed decrease of the maximum rate of air flow with the lung volume close to the residual lung volume (Fig. 1, 2). It occurred with normal value of the bronchial resistance, vital capacity of the lungs and FEV<sub>1</sub>. Thus, according to the ERF examination, bronchial spasm in the period of remission of mild BA occurs in 12% of BA patients and 42% BA patients with comorbid IBS, which is indicative of a considerable effect of comorbid IBS on the peripheral bronchi spasm in BA patients, in tract, it was manifested by increase bronchial resistance and FEV<sub>1</sub> reduced more than 80% from the appropriate one. This group of patients is characterized by a pronounced changeability of functional parameters from the norm to extreme disorders depending on the degree of BA control. The variants with incomplete reverse obstruction of the peripheral bronchi mainly, even in the period of control over BA, prevailed among patients with BA and IBS. Thus, comorbid IBS available in patients with moderate BA does not enable to control BA completely at the expense of peripheral bronchial spasm maintained, which requires pharmacological correction in the form of intensified inhalation therapy of BA. The third, the biggest group of patients with stable generalized obstruction syndrome, included all the patients suffering from COPD and COPD with IBS (Fig.1).

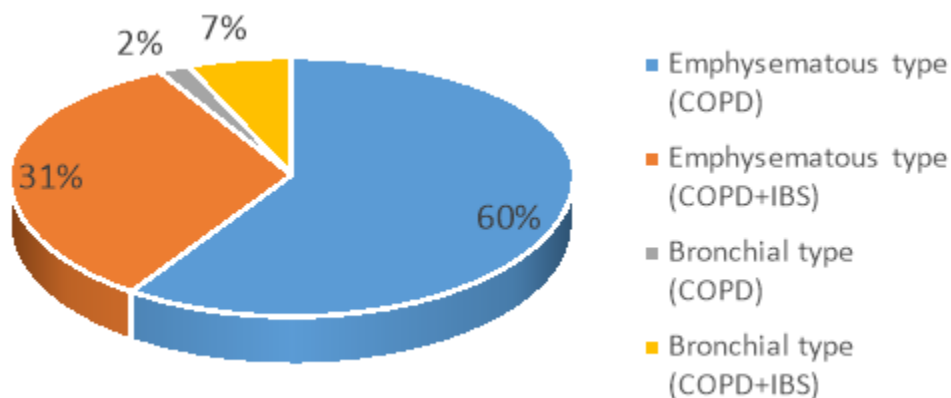


**Figure 1** Distribution of bronchial obstruction variants in BA patients.

In their turn, patients with this syndrome were divided into two subgroups: patients with bronchial and emphysematous variants of stable generalized obstruction syndrome. The emphysematous variant was characterized by relatively unchanged inspiration and peak inspiratory flow (PIR)>peak expiratory flow (PEF), prevailing increase of bronchial resistance with expiration compared with inspiration, decrease of vital capacity of the lungs. Inflammatory factor did not dominate in genesis of bronchial obstruction, but collapse of the minor bronchi resulted from the loss of elastic properties of the lungs. The bronchial variant of bronchial obstruction was characterized by an increased bronchial resistance both during inspiration and expiration, which is indicative of a prevailing role of inflammation in obstruction genesis. The vital capacity of the lungs did not change practically in comparison with FEV<sub>1</sub> and bronchial resistance (fig. 2). Bronchial variant was found in 44(88%) of patients with COPD and 47(94%) patients with COPD and IBS. Emphysematous variant was found in 11 patients with COPD (11%) and 3 (6%) patients with COPD and IBS (Fig. 3).



**Figure 2** Distribution of bronchial obstruction variants in patients with BA and IBS.



**Figure 3** Distribution of bronchial obstruction variants in patients with COPD.

The variants with prevailing peripheral and central bronchial obstruction were found as well. In case of the norm; or inconsiderable decrease of the vital lung capacity in comparison with FEV<sub>1</sub> peripheral obstruction prevailed in the structure of generalized obstruction. With considerably reduced vital lung capacity and decreased FEV<sub>1</sub> prevailing central obstruction was diagnosed in general obstruction genesis. The variants with peripheral obstruction of the minor bronchi prevailed in 42 out of 47 patients with COPD and IBS.

#### 4. DISCUSSION

To determine reversibility of obstruction the tests with inhalation bronchodilators were used. Their effect on the parameters of “flow-volume” curve was assessed, on FEV<sub>1</sub> mainly.

The bronchodilator response (BR) was assessed considering the predicted value for FEV<sub>1</sub>:

$$BR (\%) = \frac{FEV_1 \text{ dil} - FEV_1 \text{ in}}{FEV_1 \text{ pred}},$$

Where: where FEV<sub>1</sub> in – initial test score before bronchodilation,

FEV<sub>1</sub> FEV<sub>1</sub> dil – after bronchodilation test,

FEV<sub>1</sub> pred – predicted value.

The American Thoracic Society and European Respiratory Society recommend considering the response to broncholytics positive at over 12% increase in FEV<sub>1</sub>. Yet, a part of patients with COPD and BA do not demonstrate considerable increase of airflow after single inhalation of bronchodilator (Joint Task Force on Practice Parameters et al., 2005). After Salbutamol inhalation a reliable increase of FEV<sub>1</sub> was registered in all the groups of patients with COPD, though, 31(31%) patients with COPD presented only 4±2% increase of FEV<sub>1</sub>. The number of patients with COPD and IBS and inconsiderable FEV<sub>1</sub> increase after bronchodilator inhalation was 27(54%), which is reliably larger in comparison with COPD patients. It should be noted that in all the patients without considerable FEV<sub>1</sub> increase emphysematous variant of bronchial obstruction and frequent exacerbations (≥4 times a year) were registered.

The best single response to broncholytic (an average FEV<sub>1</sub> increase 19.5±2.3%) was found in BA patients with transient generalized obstruction syndrome and prevailing bronchospasm. In BA patients with IBS with transient generalized obstruction syndrome FEV<sub>1</sub> increase after broncholytic inhalation was on an average 12.6%±1.7%.

## 5. CONCLUSIONS

The analysis of ventilation respiratory function disorders found prevalence of bronchial peripheral type of stable generalized bronchial obstruction in patients suffering from COPD and IBS. Transient generalized obstruction syndrome prevailed in BA patients with IBS, completely reverse obstruction – in BA patients without IBS, and maintenance of the peripheral bronchi spasm in BA patients with IBS. Therefore, the most severe course of the disease and the worst response to the broncholytic was found among the COPD patients with IBS and considerable generalized bronchial obstruction. FEV<sub>1</sub> increase after broncholytic inhalation was the lowest in COPD patients with IBS. This category of patients requires a long anti-inflammatory therapy involving antibiotics and medicines for IBS. In BA patients with IBS and transient generalized obstruction less pronounced response to the broncholytic was found in comparison with BA patients, which is indicative of more severe course and inter-aggravation of the comorbid pathology. BA patients with IBS of a controlled course presented isolated obstruction of the minor bronchi, which is indicative of the lack of complete asthma-control.

### Acknowledgement

Authors would like to thank all participants of this study.

### Author Contributions

All authors contributed to the research and/or preparation of the manuscript.

### Funding

This study received no external funding.

### Conflict of Interest

The authors declare no conflict of interests.

### Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study.

### Ethical approval

The study was approved by the Biomedical Ethics Committee of the Bukovinian State Medical University (experimental study; Minutes No. 36 dated 17.11.2019). The article is recommended for publication by the Biomedical Ethics Committee of the Bukovinian State Medical University (Minutes No. 4 dated 22.04.2020). The state registration number is 0114U002471.

### Data and materials availability

All data associated with this study are present in the paper.



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